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SOME EXPERIMENTALLY PROVED HERBS IN PEPTIC ULCER DISEASE

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ABSTRACT

Peptic ulcer is a worldwide health problem because of its high morbidity, mortality and enormous financial implication. An estimated 15,000 deaths per year occur as a consequence of complicated PUD. A large number of drugs for peptic ulcer disease are available in mainstream medicine but they are associated with numerous side effects like arrhythmias, impotence, gynaecomastia and haematopoietic changes and the recurrence is also very common. In recent times, focus on plant research has increased all over the world and a large body of evidence has been collected to show immense potential of medicinal plants used in various traditional systems. Here, an attempt is made to summarise experimentally proved herbs used in PUD during last decade.

INTRODUCTION: Peptic ulcer disease (PUD) is one of the most common gastrointestinal disorders, which causes a high rate of morbidity [1]. It comprises both gastric and duodenal ulcers. These are benign defects in the gastrointestinal mucosa that extends beyond the muscularis mucosa, and are perpetuated by acid peptic activity. They occur commonly in the proximal duodenum or in the stomach and also occur in other areas exposed to gastric juice such as lower end of the oesophagus, Meckel's diverticulum or at the site of gastro-jejunal anastomosis [2]. In India, peptic ulcer is more prevalent in Jammu and Kashmir, followed by Southern India. North India comes next, and East and North East have comparatively lower prevalence [3]. The lifetime prevalence of peptic ulcer disease is 5 to 10 percent, with about equal prevalence in men and women.

Peptic ulcer is a worldwide health problem because of its high morbidity, mortality and enormous financial implication. An estimated 15,000 deaths per year occur as a consequence of complicated PUD [1]. Some studies have shown that duodenal ulcer is more common in the Southern part of India compared to the North [4, 5]. Peptic ulcers are uncommon in children, but the risk increases with age. Ulcers are caused by an imbalance between aggressive and defensive factors of the gastric mucosa. Gastric acid and pepsin make up the offensive factors whose proteolytic effect is buffered by mucin production, mucosal glycoprotein, cell shedding, cell proliferation and prostaglandins [6].

In India, PUD is common and the Indian Pharmaceutical industries share 6.2 billion rupees and occupy 4.3% of the market share in consuming the antacids and antiulcer drugs [5]. The incidence of ulcer disease increases with age, due to excessive use of NSAIDs and the reduction in tissue prostaglandins [6]. The therapy of peptic ulcer involves decreasing the secretion of acid with H_2-receptor antagonist or proton pump inhibitor, neutralizing secreted acid with antacids and enhancing the mucosal protection

mechanism by cytoprotective agents. The later one is being appreciated and taken up as equally important measure to that of anti-secretory agents in the management of peptic ulcer [7]. It has also become a customary that aforesaid treatments are coupled to eradicate *H. pylori* [8]. Although these drugs have brought about remarkable changes in ulcer therapy but efficacy and safety of these drugs are still debatable. Reports on clinical evaluation of these drugs show that there are incidences of relapses, adverse effects and danger of drug interactions during ulcer therapy [5, 9].

In recent times, focus on plant research has increased all over the world and a large body of evidence has been collected to show immense potential of medicinal plants used in various traditional systems. More than 13,000 plants have been studied during the last few years [10]. According to the World Health Organization, more than 80% of the world's population - primarily those of developing countries relies on plants and plant derived medicines for their health care [11]. Most of the herbal drugs used in the management of peptic ulcer have been reported to reduce the offensive factors, proved to be safe, effective and showed better patient tolerance [9, 12].

Hence, use of natural drugs alone or in combination with other drugs should be seriously considered in the management of PUD [13]. The first drug reported effective against ulcer was carbenoxolone, discovered as a result of research on a commonly used indigenous plant, *Glycyrrhiza glabra* (Mulethi) [14].

A large number of drugs for peptic ulcer disease are available in mainstream medicine but they are associated with numerous side effects like arrhythmias, impotence, gynaecomastia and haematopoietic changes and the recurrence is also very common [15]. Therefore, development of drugs which can be used safely in peptic ulcer and associated disorders assumes tremendous significance.

In modern system of medicine a number of drugs including proton pump inhibitors and H_2 receptor antagonists are available for the treatment of peptic ulcer, but clinical evaluation of these drugs has shown incidence of relapses, side effects, and drug interactions. Herbal drugs afford better protection and decrease the incidence of relapses that's why they are preferable**.**

In **Table 1 and 2,** an attempt has been made to summarize some of the important antiulcer studies done with herbal plants during the last few decades.

TABLE 1: EXTRACTS OF SOME MEDICINAL PLANTS POSSESSING ANTI-ULCEROGENIC ACTIVITY

S. No	Plant	Extracts	Models	Mode of action	Year
1.	**Sagwan** *Tectona grandis L.* (Trunk Bark & wood chips) [16]	Ethanolic fraction	PL, RS &prednisolone induced GU in rats. HIST- induced GU & DU in GP	No effect on acid secretion but caused an increase in mucin secretion.	1982
2.	**Asgand** *Withania somnifera* (Roots) [17]	SG-1 [total methanol -H2O (1:1)] SG-2 (sitoindosides VII, VIII& withaferin-A)	RS- induced GU in rats	Anti-stress activity	1987
3.	**Adrak** *Zingiber officinale* (Root) [18]	Acetone extract	HCl/ ethanol induced gastric ulceration	-	1988
4.	**Haldi** *Curcuma longa Linn.* [19]	Ethanol extract	RS & PL, Indomethacine & Reserpine induced gastric ulceration	-	1990
5.	**Sanjeevani** *Selaginella Bryopteris* [20]	Ethanolic extract	RS ulcers in rats	-	1993
6.	**Chai** *Camellia sinensis* [21]	Hot water extract	Cold + Restraint stress induced ulcers in rats	-	1995
7.	**Bhangra** *Wedelia calendulacea* (Leaves) [22]	Aqueous and ethanolic extracts	ASP- and RS- induced (antiulcer) & acetic acid (healing)- induced GU in rats	-	1996
8.	**Kranjoh** *Pongamia pinnata* (Seeds [23] & Roots) [24]	PE, AE, CE and EE extracts	RS- induced GU in mice RS & PL- induced GU in rats	Decrease in acid- pepsin & increase in mucin secretion by ethanolic extract	1997

9.	**Asal alsoos** *Glycyrrhiza glabra* [25]	Water decoction	PL- and CRS- induced GU in rats	Mucosal defensive factors by enhancing mucin secretion & life span of mucosal cells	1997
10.	**Taleespattar** *Abies pindrow* Royle (Leaves) [26]	CE, AE & EE extracts	CRS- induced GU in rats	Antistress activity	1998
11.	**Kutki** *Picrorhiza Kurroa* [27]	Ethenolic extract	HCl/ethanol induced		1999
12.	*Cissampelos muronata* [28]	Methanolic extract	Indomethacin-, HIST-, stress-induced GU		1999
13.	**Brahmi** *Bacopa monniera* [29] (Whole plant)	Fresh juice	CRS-, ethanol-, ASP- and PL-induced GU in rats	No effect on acid-pepsin secretion, increase in mucin secretion, life span of mucosal cells.	2000
14.	**Karela** *Momordica charantia Linn.* [30]	Olive oil extract	Ethanol induced		2000
15.	**Brahmi** *Centella asiatica* [31] (Whole plant)	Fresh juice	CRS-, ethanol-, ASP- and PL-induced GU in rats	No effect on acid-pepsin secretion, increase in mucin secretion & life span of mucosal cells.	2001
16.	**Heel Kalan** *A. subulatum* [32]	Methanolic extract	Ethanol induced		2001
17.	**Kela** *Musa paradisiaca* [33]	Methanolic extract	CRS- induced		2001
18.	**Sankh pushpi** *Convolvulus Pluricaulis* [34] (Whole plant)	Fresh juice	CRS-, ethanol-, ASP- and PL-induced GU in rat	No effect on acid-pepsin secretion, increase in mucin secretion & life span of mucosal cells.	2001
19.	**Sanbhalo** [35] *Vitex negundo*	Aq. Extract	Piroxicam-induced GU		2001
20.	**Amla** *Emblica officinalis* [36]	Fresh juice	CRS-, ethanol-, ASP- and PL-induced GU in rat	No effect on acid-pepsin secretion, increase in mucin secretion & life span of mucosal cells.	2002
21.	**Satawar** *Asparagus racemosus* [37]	Fresh juice	PL- and CRS- induced GU in rats	No effect on acid-pepsin secretion, increase in mucin secretion & life span of mucosal cells.	2003
22.	**Ushba Hindi** *Hemidesmus indicus* [38]	Ethanolic extract	ASP, PL	Increased mucin secretion	2003
23.	**Tulsi** *Ocimum sanctum Linn.* [39]	Ethanolic extract	CRU, AL, ASP, PL, AA, cysteamine	Has no effect on acid & pepsin but increases mucin secretion	2004
24.	*Terminalia pallida Brandis* [40]	Ethanolic extract	Indomethacin, HIST, AL	Decreases acid secretion & potent antioxidant	2005
25.	*Allophylus serratus* Kurz [41]	Ethanolic extract	CRU,AL,ASP,PL	Decreases acid secretion & peptic activity & increases mucin secretion	2005
26.	*Desmodium gangeticum* [42]	Ethanolic extract	CRU,AL,ASP,PL	Increases mucin secretion	2005
27.	**Heele Khurd** *Elletaria cardamomum* Maton [43]	Methanolic extract	ASP, ethanol, PL-induced	-	2006

AE-Acetone; ASP-Aspirin; CE-Chloroform; CRS-Cold restraint stress; CYS- Cysteamine; DU-Duodenal ulcer; EE-Ethanolic; GP-Guinea pig; GU-Gastric ulcer; HIST-Histamine; PE-Petroleum ether; PL-Pylorus ligation; RS-Restraint stress.

TABLE 2: ULCER PROTECTIVE EFFECT OF SOME ACTIVE CONSTITUENTS ISOLATED FROM HERBAL DRUGS

S. No.	Plants	Active constituents	Models	Mode of action	Year
1.	**Neem** *Azadirachta Indica* [44]	Nimbidin	ASP-, prednisolone, indomethacin-, serotonin stress- & acetic acid induced GU in rats. HIST-induced DU in GP.	-	1984
2	**Sagwan** *Tectona grandis Linn.* (Trunk bark & wood chips) [45]	Lapachol	IS- and ASP -induced GU in rats. CYS- and HIST-induced DU in rats and GP respectively.	*per se* no significant effect on both offensive &defensive factors, but reversed the ASP- induced increase in peptic activity & decrease in sialic acid & mucin secretion.	1987
3	*Rhamnus procumbens* (Whole plant) [46, 47]	Kaempferol	PL-, ethanol, IS-and CRS-induced GU in rats & HIST-induced GU & DU in GP.	Decrease in acid-pepsin secretion & increase in mucin secretion, Endogenous increase in PGs & decrease in LTs_4	1988
4.	**Shilajit** [48]	Fulvic acid, 4/-methoxy 6-carbomethoxy bi phenyl	PL-, PL+ ASP-and RS-induced GU and CYS-induced DU in rats.	*per se* decrease in acid-pepsin secretion & cell shedding, tendency to increase mucin secretion but reversed the increase in cell shedding & decrease in mucin secretion induced by ASP.	1988
5.	*Rhamnus triquerta Wall* (Whole plant) [49]	Emodin	RS-, PL- and IS- induced GU in rats	Decrease in acid-pepsin secretion & increase in mucin secretion in ASP-treated group.	1991
6.	*Picrasma quassioides* [50]	MeOH extract, CHCl3 soluble fraction, Nigakilacetone , Methynigakinone	ASP- induced GU in rats	-	1994
7.	**Dhatura** *Datura fastuosa* (Leaves) [51, 52]	Withafastuosin-E	CRS-, PL- and ASP induced GU in rats	*per se* decrease in acid-pepsin and no effects on mucin secretion, mucosal cell shedding, proliferation and glycoproteins significant increase in endogenous PGs.	1997
8.	**Bael** *Aegle marmelos Correa* (Seeds) [53]	Luvangetin	PL-and ASP- induced GU in rats and CRS- induced GU in rats and GP.	-	1997
9.	*Flueggea microcarpa* (Leaves & roots) [53]	Bergenin/Norbergenin	PL-and ASP- induced GU in rats and CRS- induced GU in rats and GP.	Increase in endogenous PGs.	1997
10.	**Tulsi** *Ocimum basilum* [54]	Fixed oil	ASP-, indomethacin-, ethanol, HIST-, reserpine, Serotonin- PL- and stress induced, GU in rats	Antisecretory	1999
11.	**Brahmi** *Bacopa monniera* (Whole plant) [55]	Standardized extract of bacoside A (35%)	CRS-, ethanol, ASP- and PL-induced GU in rats	No effect on acid-pepsin secretion, increase in mucin secretion and life span of mucosal cells.	2001

AE-Acetone; ASP-Aspirin; CE-Chloroform; CRS-Cold restraint stress; CYS-Cysteamine; DU-Duodenal ulcer; EE-Ethanolic; GP-Guinea pig; GU-Gastric ulcer; HIST-Histamine; IS-Immobilization stress; PE-Petroleum ether; PL-Pylorus ligation; RS-Restraint stress;

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